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USE IN MALES (NPPABNRM)

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13. ABSTRACT (Maximum 200 words) A Neurophysiological Performance Assessment Test (NPAT) battery of sensory and cognitive event-related potential (ERP) tasks was designed by the Office of Military Performance Assessment Technology (OPMAT). Test-retest reliability data for cognitive ERPs for tasks in this battery was obtained from 37 normal subjects. The test-retest reliability of N1, P2 and P3 components of cognitive event-related potential were determined for the auditory rare event monitoring task, two Continuous Performance tasks and the Sternberg Memory task with two set sizes. The Cronbach alpha coefficient was used to test within day (2 tests on the same day) and between day reliability. The test-retest reliability of the ERP components recorded in this battery of tasks was high (.7 to .9). The reliability of the P3 amplitude measurements exceeded the reliability of the percent correct values in all tasks except the Sternberg memory task with a three letter set size. The measurement of the ERP components, in particular the P3, in this battery of cognitive tasks appears stable enough to build norms for the ERPs components for each of the tasks in the battery. Such normative ERP data will be useful in the application of NPAT battery. Not only was the test-reliability of the ERPs data high, but in using this normative ERP data we were able to identify cognitive processing alterations in a group of drug abusers (N=10) who denied illicit drug use.				
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FOREWORD

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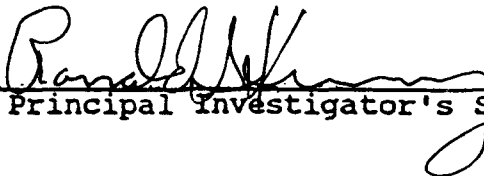
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For the protection of human subjects, the investigator(s) have adhered to policies of applicable Federal Law 45CFR46.

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FINAL REPORT

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7. **Project Title:** Performance Norms on NPPAB for Limited Drug Use in Males (NPPABNRM)
8. **Current Staff with percent of effort on each project.**
Herning, R.I.- 50% Guo, X -30%
Koepl, B -30% Graber, E. (unpaid volunteer)-10%

9. **Approximately PI expenditures 1 Sept 1991 to date:**

Personal Services: 0 Travel: 0

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10. **Comments on administrative and logistical matters:**

Both Dr. Brigham and Ms. Glover, who were responsible for subject testing, left the project in 1991. The loss of key personnel made it impossible to continue testing on this project at that time. Testing was further delayed when the acting Etiology Branch chief was replaced by a permanent chief. In October 1992, Dr. Herning was transferred to the Medical Affairs Branch where the project was completed.

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Introduction

The use of Event Related Potential (ERP) methodology in the assessment of cognitive processing and performance has excellent potential. Sensory and cognitive stages of human information processing can be directly measured by brain potentials during cognitive tasks. These ERP measures complement more traditional measures of reaction time and correctness. Brain potentials are related to cognitive processes as such as selective attention (Hanson & Hillyard, 1980; Naatanen et al., 1993; Teder et al., 1993), working memory (Gevin & Cutillo, 1993), stimulus evaluation (Donchin & Coles, 1988; Polich, 1989) and other aspects of information processing (Johnson, 1993). The brain potentials are sensitive to the effects of drugs (Herning et al., 1979; 1985, 1987; Coons et al., 1981; Peloquin and Klorman, 1986; Brunaghin et al., 1987; Fitzpatrick et al., 1988), fatigue or habituation (Knott, 1985; Ditraglia & Polich, 1991), changes in dual task performance (Wickens et al., 1983) and other conditions of interest to the military.

The ERP methodology is not new. Its application to military performance questions is, likewise, not new. Its application to applied problems has suffered from a lack of standardization of task parameters, ERP recording procedures and thorough characterization of the subject populations.

Some guidelines for standardization were outlined under the Office of Military Performance Assessment Technology (OPMAT). A test battery of sensory and cognitive ERP tasks was designed with

specific stimulus parameters and recording procedures (Reeves et al., 1991). The sensory ERP paradigms have norms since they are also used in clinical diagnosis of medical disease. Test-retest reliability was been reported for the auditory rare event monitoring task or oddball task as it is often called (Sklare & Lynn, 1984; Polich, 1986; Fabianai et al., 1987; Segalowitz & Barnes, 1993), but not the other cognitive tasks. Whether or not norms for cognitive ERPs can be constructed remains unclear. This project was designed to collect normative ERP data on some of neurophysiologic cognitive tasks specified in the OMPAT, Level 1, battery as well as provide test-retest reliability data on normal non-drug using males. The project was extended to females.

The research plan called for testing 40 to 50 non-drug using subjects on four tasks from the Neurophysiologic Workload Test Battery (NWTB). The tasks included the Auditory Rare Event Monitoring Task, the Continuous Performance Task (two versions) and the Sternberg Memory Task with two memory loads. These cognitive ERP tasks were administered and ERP data was collected using OPMAT guidelines. In addition, DSM-III-R interviews and other psychometric testing were obtained to screen for current psychiatric illness and drug use. An urine toxicology for illicit drugs was also obtained. Half of the subjects were tested on two day study to evaluate the test-retest reliability of these brain potentials over two test days. The other half of the subjects were tested to evaluate test-retest reliability on the same day. The ERP data from the first day of the two day study will be combined

with the one study to increase the sample size.

The collection of normative ERP data on non-drug using persons is complicated by cigarette smoking. While nicotine is certainly is a drug, normative ERP data on smokers who do not use other drugs is of importance. Nicotine is particular problematic since the effects of nicotine deprivation on the EEG and performance and their reversal by smoking are well documented (Knott, 1985). We proposed to extend our collection of normative cognitive ERP data to include non-deprived smokers. We feel the development of norms on these cognitive tasks for both smokers and non smokers may increase the success of this project by reducing the variability in the otherwise non-drug using group.

Methods

Subjects

Fifty-six subjects passed a screening interview designed and administered by Nova Research, a contractor responsible for obtaining human subjects for research at the Addiction Research Center. Nine subjects of these subjects failed show up for testing or were screened out for current psychiatric problems using the Computerized Diagnostic Interview, Revised (CDISR: Blouin, 1985) with a followup interview or NIMH Diagnostic Interview Schedule, Version III Revised (DSM-IIIR: Robins et al., 1989). Since the urine toxicologies lagged behind ERP testing, ten additional

subjects, who reported no illicit drug use, but had positive urine toxicologies were tested on first day of ERP test battery. The ERP and performance data from this group were compared to the non-drug using subjects, but the data was not used in the test-retest reliability calculations.

Thus, we collected normative ERP data on 37 subjects who (1) had no current Axis I (except nicotine dependence) or Axis II diagnosis as determined by an interview using DSM-III-R criteria, (2) were healthy (health history interview given by a nurse or counsellor) and (3) had a negative urine toxicology screen for amphetamine, barbiturates, benzodiazepines, cocaine, opiates, phencyclidine and cannabinoids. The mean age of the sample was 27.5 years (5.6 years standard deviation) and the mean years of formal education was 12.5 years (2.1 years standard deviation). Eighteen males and nineteen females were tested. Twenty of the 37 subjects were tested on the cognitive ERP tasks (Auditory Rare Event Monitoring Task, two Continuous Performance Tasks, Sternberg Memory Task (2 set sizes) on two different days with two test sessions each day. The remaining subjects were tested on the one day test-retest procedure using the same tasks administered twice on the same day. Sixteen of the 37 subjects were nicotine dependent and were allowed to smoke if they chose to any time during the study except during of the 25 minute test battery. They were asked if they wanted to smoke before and after the ERP test battery.

Experimental Procedures

On each day of ERP testing, the subjects completed the St. Mary's Sleep Questionnaire, the Profile of Mood State questionnaire and the Beck Depression Inventory. We evaluated test-retest reliability of the ERP measures on the same day and between test days. On the first day test day, the subjects were instructed on the tasks and given a practice test before the actual test session. One hour after the start of the first test session they were retested on each task in the battery. The second test day was similar except that there were no practice sessions.

Cognitive Information Processing Tasks. In the Auditory Rare Event Monitoring (AREM) Task, tones were delivered binaurally through TDH-39 earphones. The subject was required to count rare tones from a series of 1000 Hz and 2000 Hz tones (80 dB SPL, 50 ms in duration, 2.0 s between tones). The 1000 Hz or rare tones occurred about 20% of the time. After the subject heard the series of tones for four minutes, he reported his count to the researcher at the end of the session. A practice session preceded the first formal test session. The N100, P200 and P300 of AREM were measured from the frequent and rare tone ERP. The ERP peaks were measured in the following latency ranges: N100 (50-180 ms), P200 (100-250 ms) and P300 (250-700 ms).

The Sternberg Memory Task was originally developed by Sternberg (1975). In this task, evoked responses were elicited visually by presenting the letter on a TV monitor. The subject was required to memorize three or six letter sets which appeared on the

monitor for 30 seconds. A series of probe letters was then displayed on the screen, one at a time. The probe letters subtended 10° of visual angle, remained on the screen for 600 ms and were presented at a rate of one every two seconds. The mean luminance of the screen was 40 cd/m^2 . If the probe letter was one that was part of the memory set, then the subjects were instructed to press a button with their preferred hand. When a presented letter was not in the memory set, then the subjects were required to press a button with their non preferred hand. A practice session preceded the first formal test session. P200 and P300 components of the Sternberg Memory Task were measured using the same latency ranges as the AREM Task. Task performance was evaluated by reaction time and percent correct.

Two Continuous Performance Tasks (CPT) were also performed. They were not in the OPMAT, Level 1, battery. The first CRT task or CPT-X was similar to the Sternberg Memory Task with a one letter memory set. During this task the subjects were required to press the push button with their preferred hand when they saw an X on the TV monitor. The stimulus characteristics were identical to the Sternberg task. No practice session was given. The second CPT task was the Paired Letter CPT. During this task the subjects were required to press the push button with their preferred hand when they saw an letter repeat (two of the same letter in a row) on the TV monitor. The stimulus characteristics were identical to the Sternberg task and no practice session was given. The P200 and P300 components of the visual ERP were measured an in the Sternberg

Memory Task. Task performance was evaluated by reaction time and percent correct.

ERP Recording and Measurement. The ERPs were recorded from F_z , C_z , and P_z (the International 10-20 System: Jasper, 1958). The reference electrode was on right ear tip. Electrooculogram (EOG) was recorded from side of the left eye and from above the left eye referred to the left ear tip in order to monitor eye movement artifacts. Isoground electrode was placed on forehead. Silver/silver chloride electrodes were used at all locations. Each electrode impedance was kept below 10 K ohm. Trials with EOG artifact were rejected. Testing was performed in a sound attenuated, electrically shielded chamber. The EEG and EOG were recorded with Grass (Model 75P11) amplifiers with a .1 to 100 Hz half amplitude band pass and a 60 Hz notch filter. The EEG and EOG channels were sampled at 200 Hz/channel with 8 microsecond interchannel delay. Single trial EEG and EOG data was saved on line. The EEG and EOG were processed for artifact and averaged after the test session. The target and non-target stimuli were averaged separately for each task.

Statistical Analysis. Separate Analyses of Variance (ANOVA) were performed on each ERP and performance measure from the four tasks (AREM, CRT-X, CPT-Paired Letter, Sternberg Memory Task). These ANOVAs were used to test for significant differences between test sessions within a day ($N=37$) and between test days ($N=20$). Each ANOVA included the between subject (nonsmoker versus smoker) factor and within subject factors: stimulus type (target versus

non- target), set size (3 versus 6 letter, Sternberg Task only) and electrode (F_z , C_z , P_z). The ANOVAs also guided in the calculation of the reliability coefficients. If the smokers and non-smokers significantly differed, separate coefficients would be calculated for each group.

Tests of the assumptions for within subject ANOVAs were made as recommended by Vasey and Thayer (1987) and corrected probability values (Greenhouse & Geisser, 1959) are reported in all cases.

The test-retest reliability of the ERPs collected in each of the tasks was determined with the intraclass reliability coefficient (Winer, 1972) and Cronbach's alpha coefficient (Nunnally, 1978). Both analyses were similar and we report only the alpha coefficients.

Finally, the ERPs and performance of the drug abusers who denied using illicit drugs were compared to that of non-drug using subjects. This analysis was not originally planned, this group is of interest to both the military and the ARC. These subjects denied using drugs on three occasions (telephone interview, on site screening interview and the psychiatric interview), but they had illicit drugs in their urine the day that they were tested on the ERP test battery. Thus, they provided a comparison group who might have altered ERPs and performance.

Results

Comparison of Non-Smokers with Smokers. Of the many

statistical tests made in the one day and two day comparisons, few significant differences were noted between non-smokers and smokers (the group factor) in the ERP components. The smokers differed from non-smokers on the amplitude of the P2 component of the ERP in the visual tasks. For P2 amplitude in the CPT-X and CPT-Paired Letter tasks, the group main effect was significant for the one day ($p < .01$) and a number of interactions involving group were statistically significant for the two day comparisons. P2 amplitude for the smokers was larger than the non smokers. P2 latency was also longer for the smokers than the non-smokers in the CPT-X task (significant main effect for group), in the CPT-Pair letter task (significant main effect for group) and in the Sternberg task (significant group by electrode interaction). For N1 latency, the group by test time by electrode interaction was significant for two day ($p < .01$), but not the one day comparisons in the AREM task. For P3 amplitude in the CPT-Paired Letter task, the group by day by time interaction was a significant in the two day comparison, but there was not indication of group differences in P3 amplitude in the one test where the sample size was larger.

Comparisons between Test Times. Within day statistically significant differences between test sessions were observed only for P2 amplitude or latency in all tests. However, no differences were observed between test session for N1 amplitude, N1 latency, P3 amplitude, P3 latency, reaction time and percent correct. P3 amplitude and latency at the P_z for the target stimulus in all the tasks is plotted in Figures 1 and 2 respectively. Reaction time to

P3 Amplitude

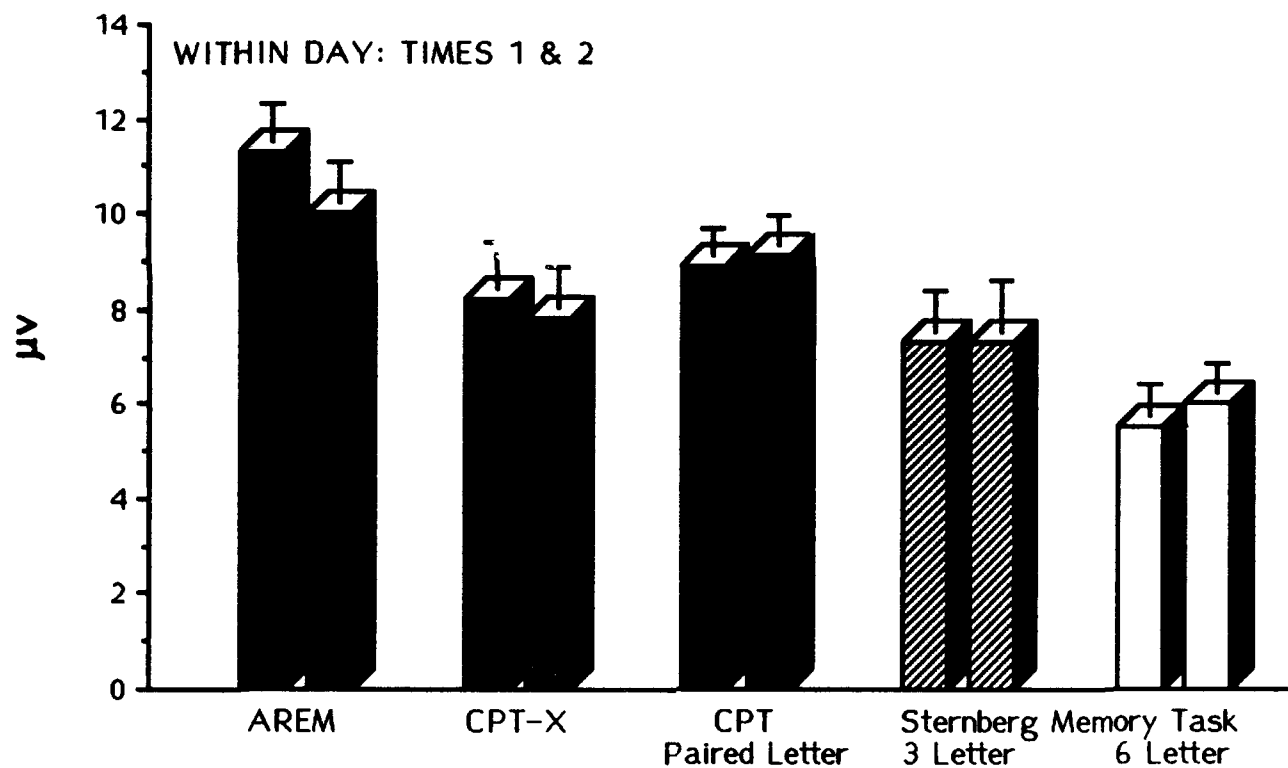


Figure 1. P3 amplitude at Pz is plotted for each task. Bars are standard errors. The left column of each pair is time 1. The right is time 2.

P3 Latency

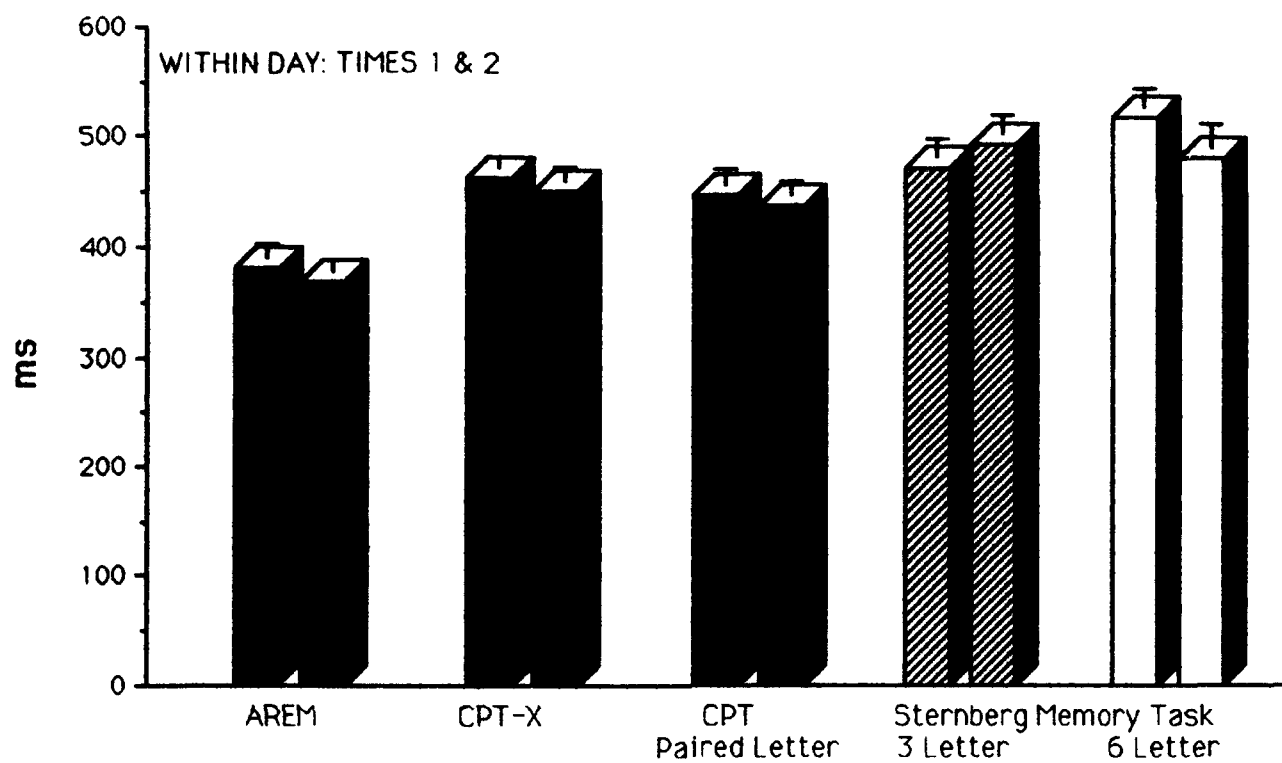


Figure 2. P3 latency at Pz is plotted for each task. Bars are standard errors. The left column of each pair is time 1. The right is time 2.

REACTION TIME

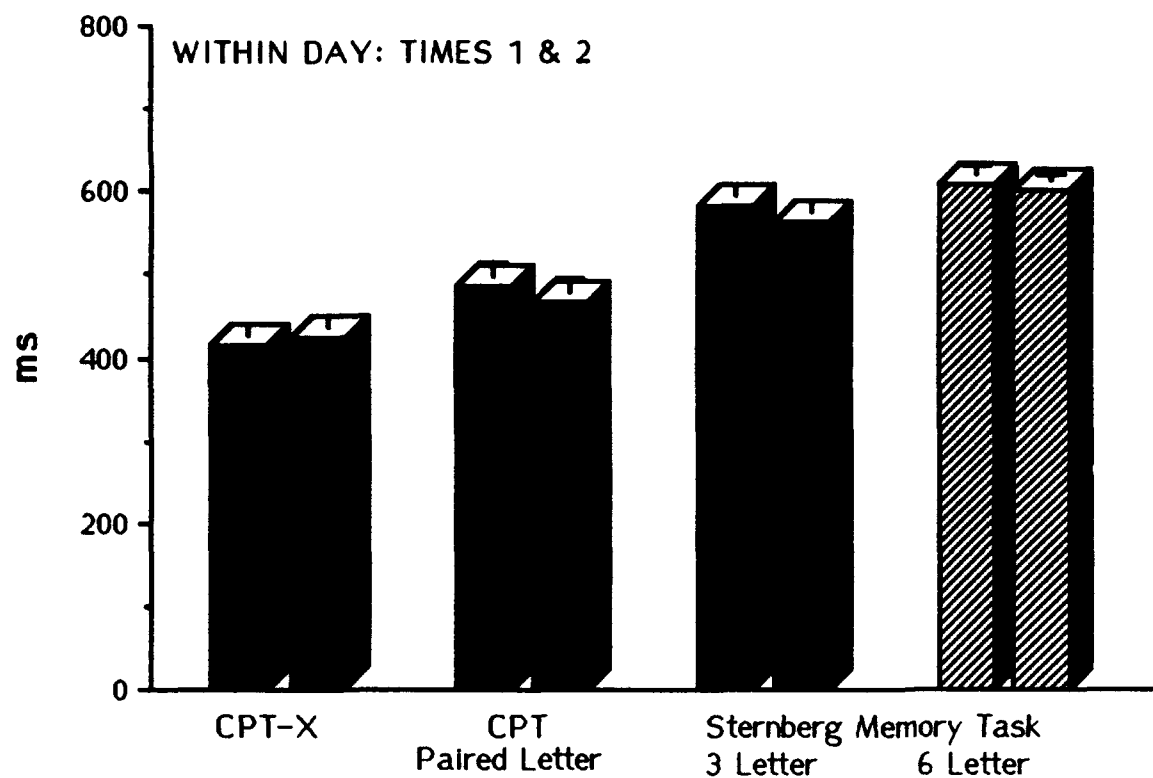


Figure 3. Reaction time is plotted for each task. Bars are standard errors. The left column of each pair is time 1. The right is time 2.

PERCENT CORRECT

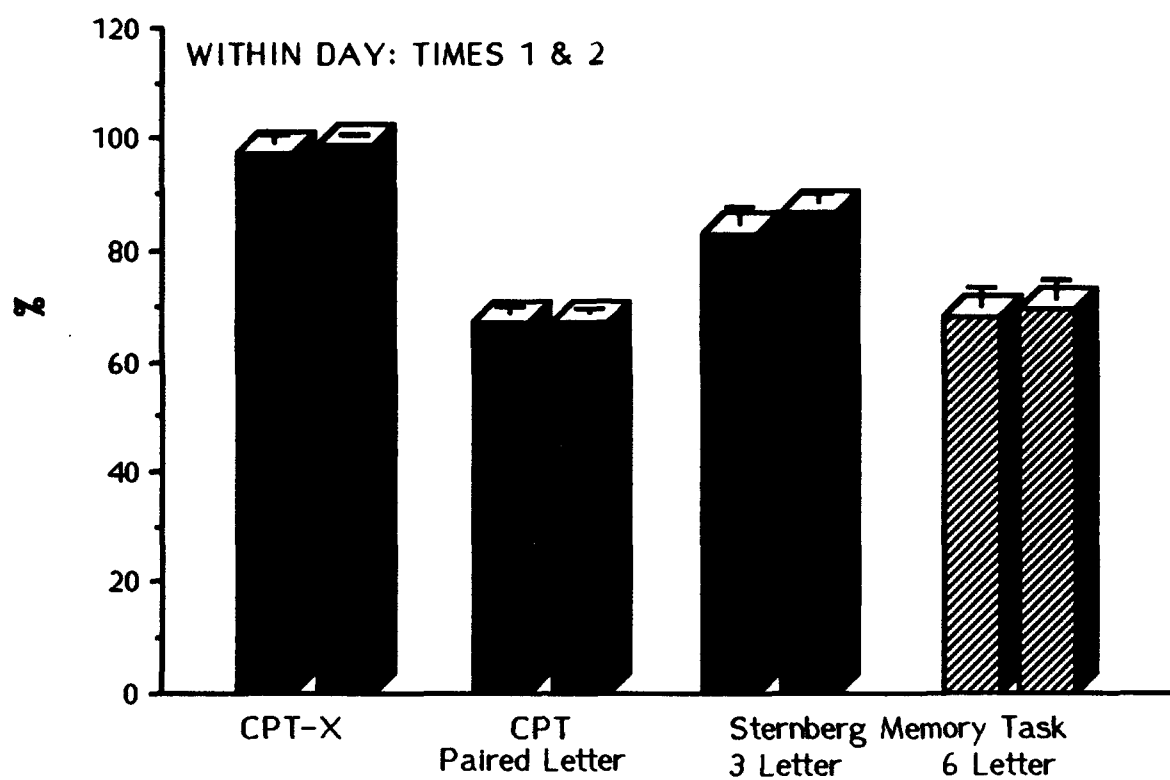


Figure 4. Percent correct is plotted for each task. Bars are standard errors. The left column of each pair is time 1. The right is time 2.

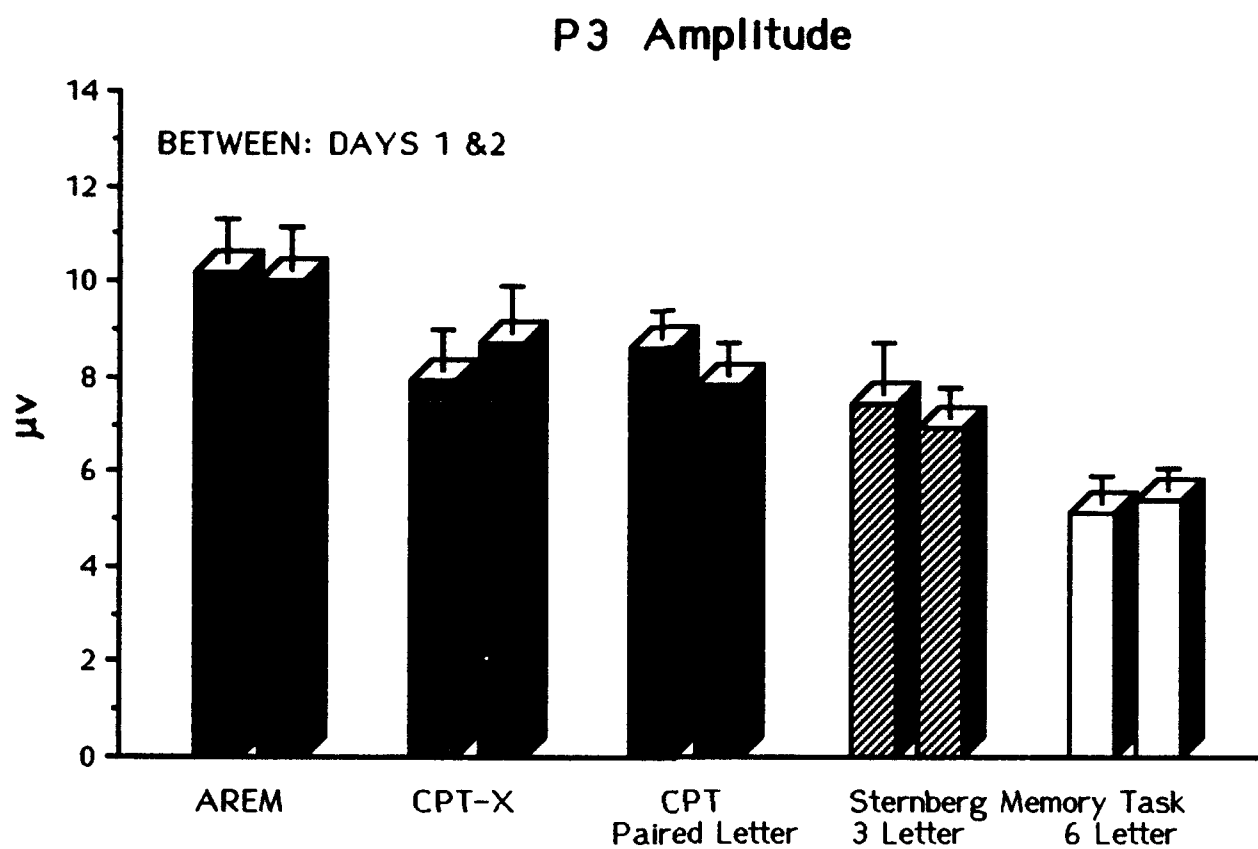


Figure 5. P3 amplitude at Pz is plotted for each task. Bars are standard errors. The left column of each pair is day 1. The right is day 2.

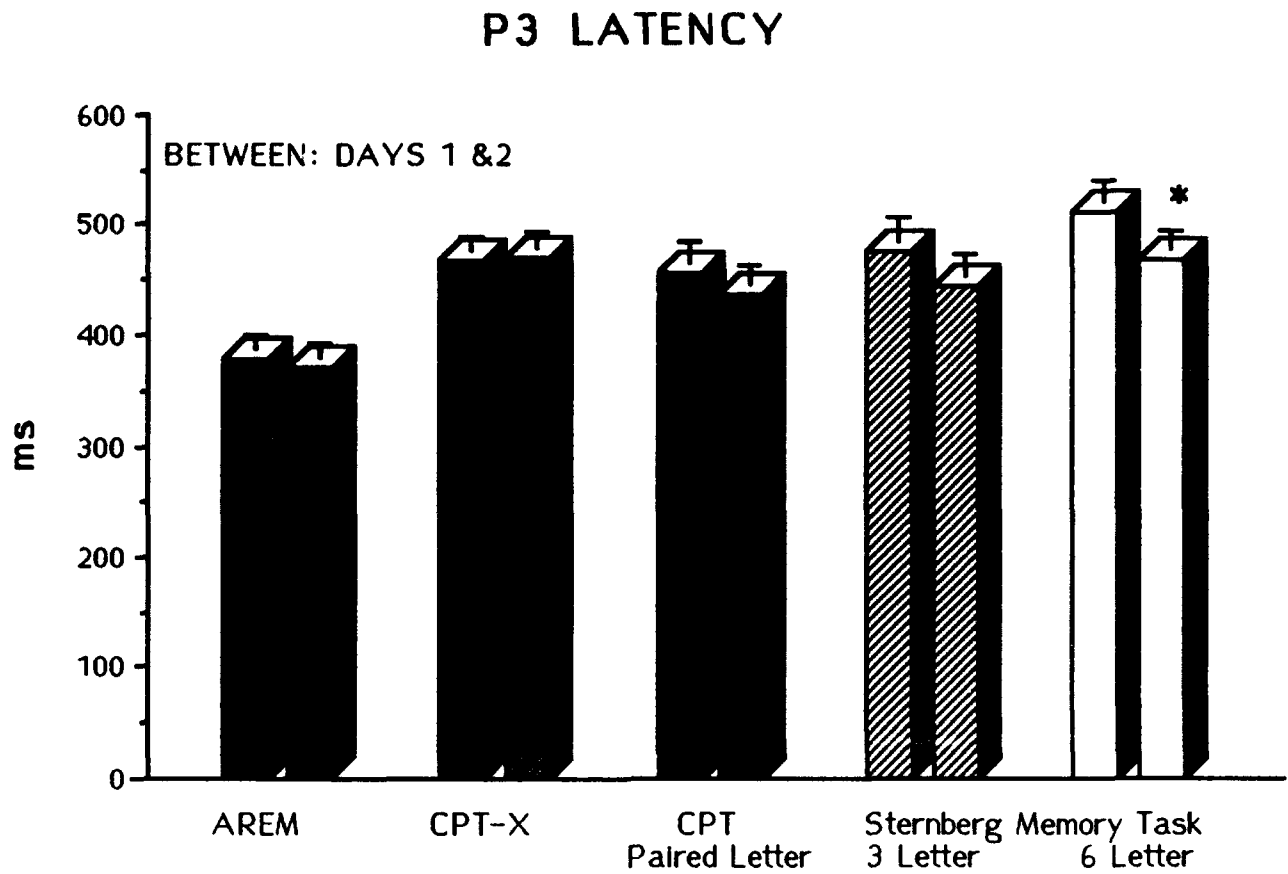


Figure 6. P3 latency at Pz is plotted for each task. Bars are standard errors. The left column of each pair is day 1. The right is day 2. The star indicates a significant difference between test days ($p < .05$).

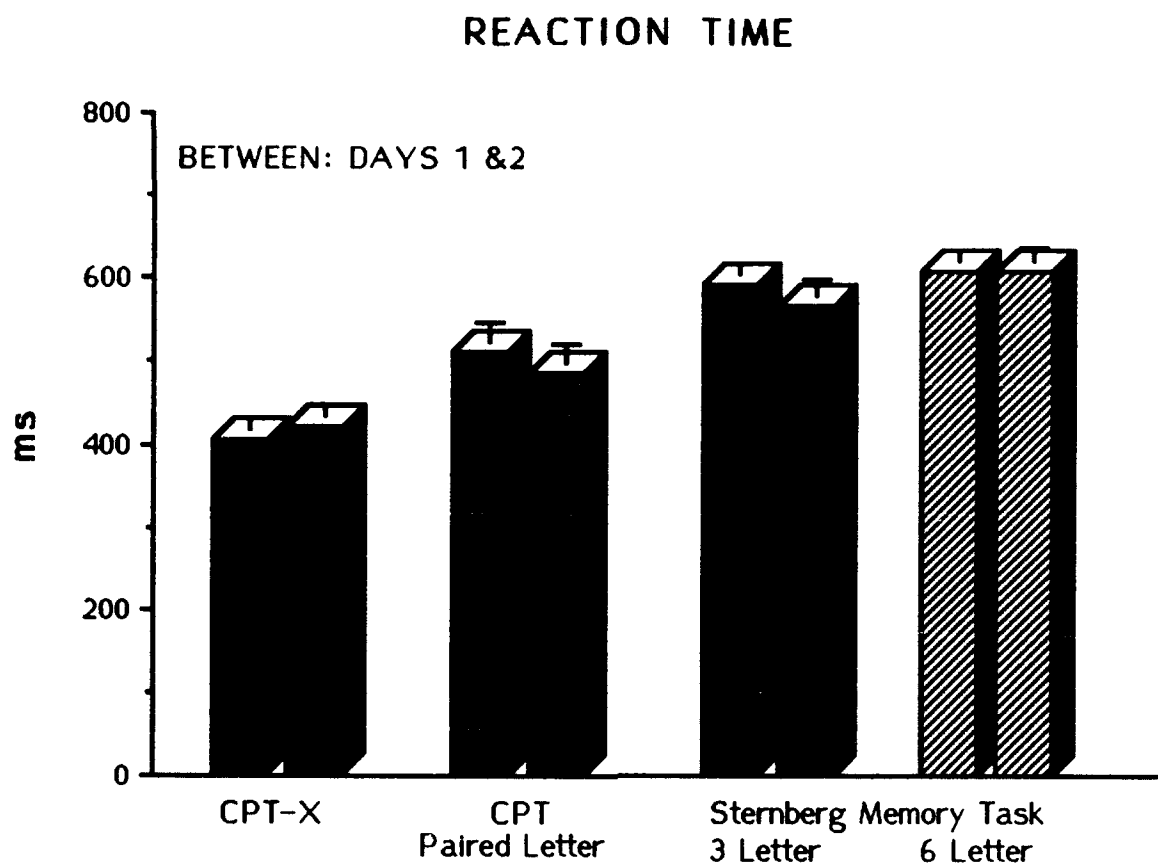


Figure 7. Reaction time is plotted for each task. Bars are standard errors. The left column of each pair is day 1. The right is day 2.

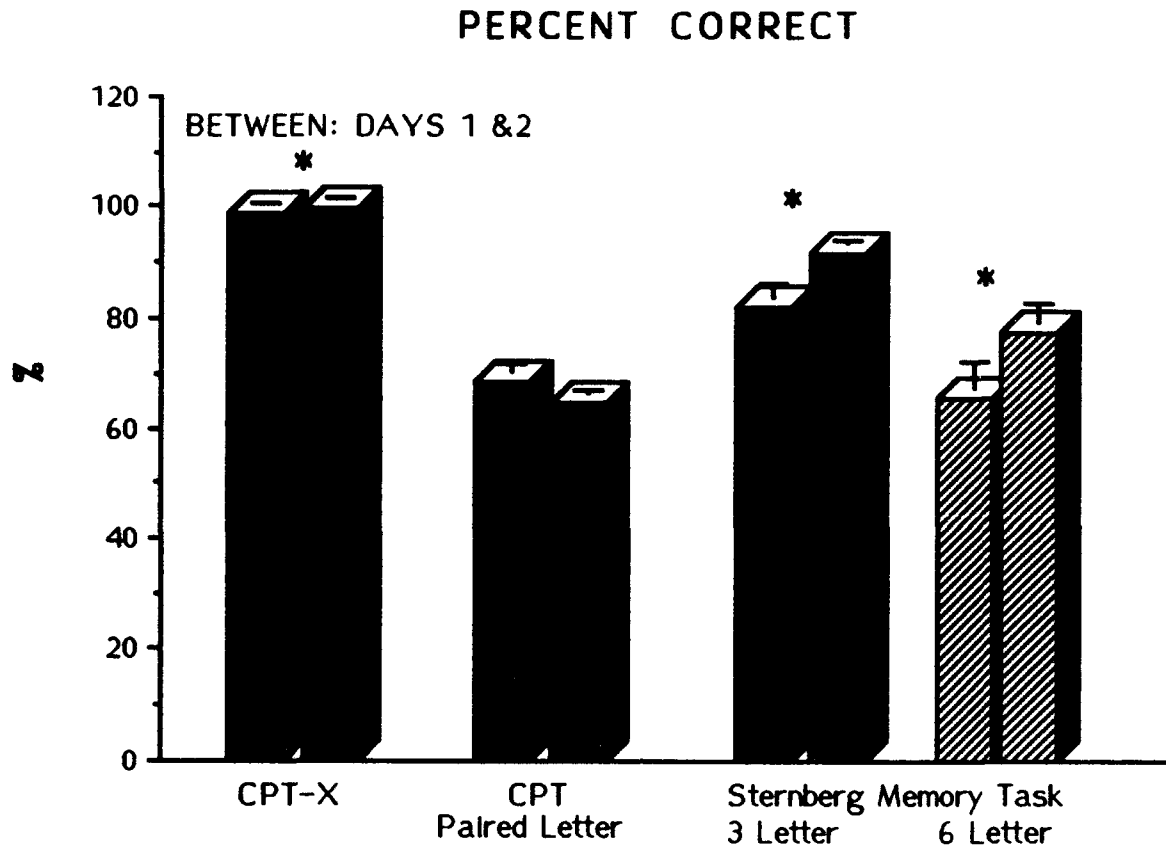


Figure 8. Percent correct is plotted for each task. Bars are standard errors. The left column of each pair is day 1. The right is day 2. Stars indicate a significant difference between days ($p < .05$).

the target stimulus and percent correct is plotted in Figures 3 and 4.

Comparisons between Test Days. Statistically significant differences between test days were observed only for P2 amplitude or latency on all tests. However, no differences were observed between test days for N1 amplitude, N1 latency, P3 amplitude, P3 latency, reaction time and percent correct. P3 amplitude and latency at the P_z for the target stimulus in all the tasks is plotted in Figures 5 and 6 respectively. Reaction time to the target stimulus and percent correct is plotted in Figures 7 and 8.

Reliability Estimates for ERP and Performance Data. The alpha reliability coefficients for the two test times on the same day are listed in Table 1. Included in the table are ERP measures for the target stimulus. The reliability was also list for the reaction time and percent correct measures. Most often the reliability of the amplitude of the ERP component was higher than that of the latency. The reliability coefficients for ERP amplitude measures ranged to .4465 to .8251. The Sternberg Memory task with set size 3 had the lowest values. P2 amplitude, likewise, had the lower values than other ERP amplitude measures. The alpha reliability coefficients for the between day comparisons for the ERP and performance measures are listed in Table 2. Lower reliability values were observed for N1 and P2 amplitude as compared to P3 amplitude. Except for the Sternberg Memory task with set size 3, the reliability coefficients for P3 amplitude ranged from .7714 to .9015 across the cognitive tasks.

Table 1
Alpha Reliability Coefficients for
Measures On the Same Day (N=37)

AREM Task

N1 at F _z Amplitude	.7837	Latency	.6102
P2 at C _z Amplitude	.6516	Latency	.6009
P3 at P _z Amplitude	.7284	Latency	.6089

CPT-X Task

P2 at C _z Amplitude	.7539	Latency	.5650
P3 at P _z Amplitude	.7629	Latency	.6108
Percent Correct	.2714		
Reaction Time	.8375		

CPT-Paired Letter Task

P2 at C _z Amplitude	.8046	Latency	-.4088
P3 at P _z Amplitude	.7836	Latency	.8755
Percent Correct	.7780		
Reaction Time	.8618		

Sternberg Memory Task

Set Size 3

P2 at C _z Amplitude	.4465	Latency	.4978
P3 at P _z Amplitude	.5606	Latency	.5053
Percent Correct	.7216		
Reaction Time	.8233		

Set Size 6

P2 at C _z Amplitude	.6755	Latency	.5909
P3 at P _z Amplitude	.8251	Latency	.5405
Percent Correct	.8119		
Reaction Time	.9017		

Table 2
Alpha Reliability Coefficients for
Measures between Days (N=20)

AREM Task

N1 at F _z Amplitude	.5667	Latency	.8928
P2 at C _z Amplitude	.5031	Latency	.6995
P3 at P _z Amplitude	.8364	Latency	.5723

CPT-X Task

P2 at C _z Amplitude	.6631	Latency	.1627
P3 at P _z Amplitude	.9015	Latency	.5914
Percent Correct	.6860		
Reaction Time	.8713		

CPT-Paired Letter Task

P2 at C _z Amplitude	.6298	Latency	.7425
P3 at P _z Amplitude	.7845	Latency	.4505
Percent Correct	.6173		
Reaction Time	.8607		

Sternberg Memory Task

Set Size 3

P2 at C _z Amplitude	.6589	Latency	.3983
P3 at P _z Amplitude	.6868	Latency	.8157
Percent Correct	.6770		
Reaction Time	.7503		

Set Size 6

P2 at C _z Amplitude	.1710	Latency	-.0711
P3 at P _z Amplitude	.7714	Latency	.4868
Percent Correct	.7234		
Reaction Time	.7533		

Comparison of ERPs from Normal Subjects with Subjects Who Used Drugs. ERP differences in the ERPs and performance measures were observed between the normal subjects (non-smokers and smokers) and drug abusers who denied illicit drug use. On all tasks reaction time was significantly longer for the drug abusers (CPT-X: group main effect [$p < .05$]; CPT-Paired Letter: group main effect [$p < .001$]; Sternberg: group by set by condition interaction [$p < .05$]). P3 amplitude differed among the three groups on the AREM (group by time by electrode interaction, $p < .05$) and CRT-X (group main effect, $p < .01$) tasks. The P3 amplitude data for the P_z electrode is plotted in Figure 9. While the P3 amplitude for the non-smokers and smokers drops slightly from the first to the second test, P3 amplitude for the drug abusers is low at the first test time and is significantly increased at the second test time. The drug abusers have the smallest P3 of the three groups in the CPT-X task.

Discussion and Conclusions

The test-retest reliability of N1, P2 and P3 components of cognitive event-related potential were determined for the auditory rare event monitoring task (Oddball task), two Continuous Performance Tasks (CPT-X: respond for an X; CPT-Paired Letter: respond to any letter which repeats) and the Sternberg Memory task with three and six letter memory sets. The Cronbach alpha coefficient was used to test within day (2 tests on the same day) and between day reliability. The alpha was .70 or higher for P3 amplitude for all tasks in both the within and

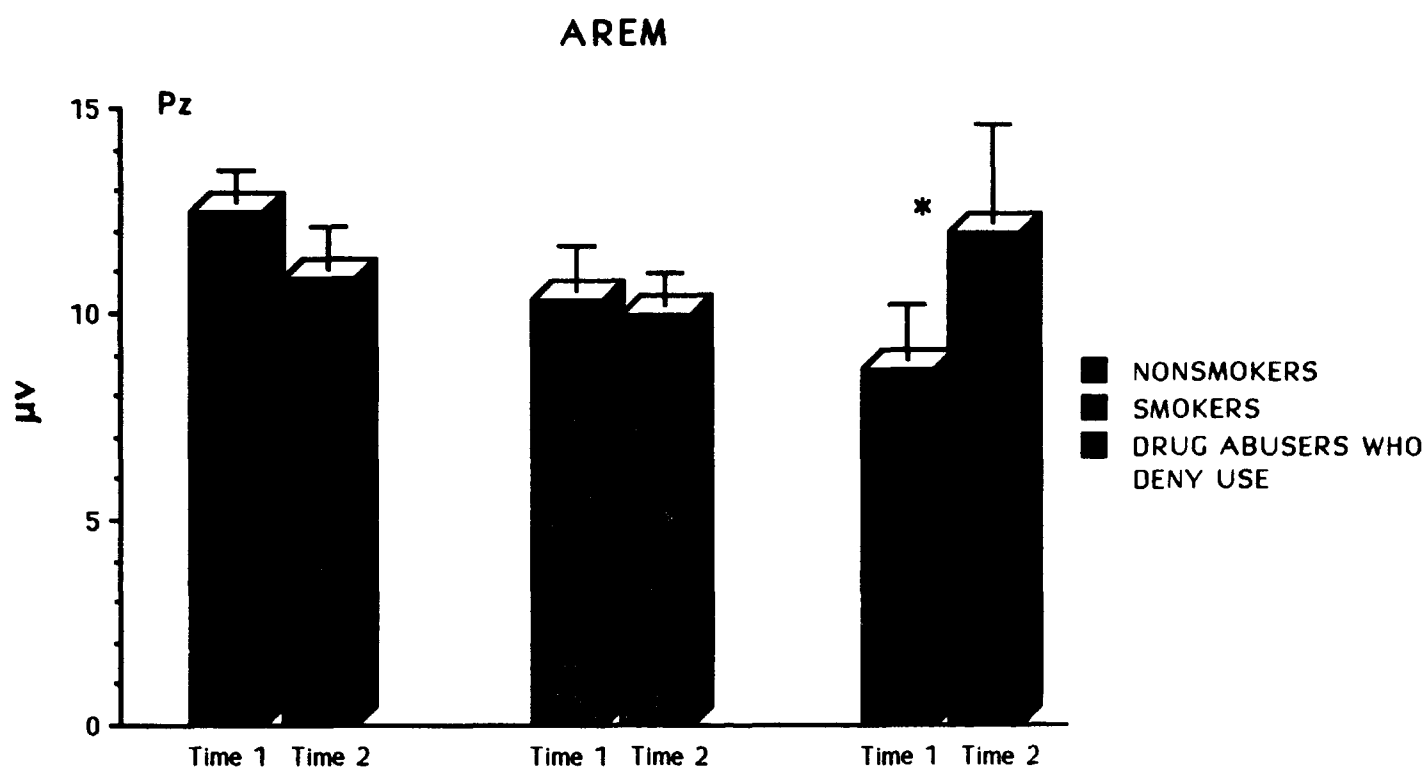


Figure 9. P3 amplitude is plotted for the 3 groups of subjects. Bars are standard errors. The star indicates a significant difference between time 1 and time 2 for the drug abusers.

between day comparisons except for the Sternberg memory task with a three letter set. The reliability of P3 amplitude in these four tasks compare favorably with previously reported findings on the Oddball task (Polich, 1986; Fabiani et al, 1987; Segalowitz and Barnes, 1993). We are the first to report reliability measures for ERP components for other three cognitive tasks. The reliability of P3 latency (.54-.87 within day, .45-.81 between days) over our four tasks, likewise, is similar to data published by the same researchers for the Oddball task.

Only Segalowitz and Barnes (1993) tested the reliability of the N1 and P2. Our reliability values for both amplitude and latency of these components were higher than those Segalowitz and Barnes reported, but lower than we found for P3 amplitude. P2 amplitude was found to significantly differ between the non-smokers and non-deprived smokers in our sample. P3 amplitude did not. Thus, the lower reliability values for P2 amplitude in our sample and those in Segalowitz study may be due to the increased variability resulting from smoking status.

When the low reliability values for the Sternberg memory task with a three letter set size are not considered, comparisons can be made among the within and between day alpha measures. N1 and P2 amplitude measurements were more reliable when made on the same day. P3 amplitude measures are more reliable when measured across days than within a day for the Oddball and both CPT tasks. No clear patterns were observed for N1, P2 and P3 latency.

The reliability of the P3 amplitude measurements exceeded the

reliability of the percent correct values in all tasks except the Sternberg memory task with a three letter set size. The reliability of reaction time measurements most often were higher than similar values for P3 amplitude and latency. However, Donchin and Coles (1988) have suggested that P3 latency and reaction time may be independent. Thus, the comparison of P3 and reaction time may not be appropriate.

The normative ERP data collected in this study proved useful when it was compared to ERPs collected from the group of drug abusers who denied using illicit drug during the screening process for this study. The test-retest pattern for the drug abusers significantly differed from non-smokers and cigarette smokers who did not use illicit drugs. Not only was the test-reliability of the ERPs data high, but in using this normative ERP data we were able to indentify cognitive processing alterations in a group of drug abuser who denied illict drug use.

In conclusion, the test-retest reliability of the ERP components recorded in this battery of four different cognitive tasks is high and comparable with data collected by other researchers on only a single task. The measurement of the ERP components, in particular the P3, in this battery of cognitive tasks appears stable enough to build norms for the ERPs components for each of the tasks in the battery.

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